

Spontaneous emergence of catalytic cycles with colloidal spheres

Zorana Zeravcic^{a,b,c,d,1} and Michael P. Brenner^{c,d}

^aSoft Matter and Chemistry Department, École Supérieure de Physique et de Chimie Industrielles de la Ville de Paris, Paris Sciences et Lettres Research University, 75005 Paris, France; ^bLiving Matter Laboratory, The Rockefeller University, New York, NY 10065; ^cHarvard John A. Paulson School of Engineering and Applied Sciences, Harvard University, Cambridge, MA 02138; and ^dKavli Institute of Bionano Science and Technology, Harvard University, Cambridge, MA 02138

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Colloidal particles endowed with specific time-dependent interactions are a promising route for realizing artificial materials that have the properties of living ones. Previous work has demonstrated how this system can give rise to self-replication. Here, we introduce the process of colloidal catalysis, in which clusters of particles catalyze the creation of other clusters through templating reactions. Surprisingly, we find that simple templating rules generically lead to the production of huge numbers of clusters. The templating reactions among this sea of clusters give rise to an exponentially growing catalytic cycle, a specific realization of Dyson's notion of an exponentially growing metabolism. We demonstrate this behavior with a fixed set of interactions between particles chosen to allow a catalysis of a specific six-particle cluster from a specific seven-particle cluster, yet giving rise to the catalytic production of a sea of clusters of sizes between 2 and 11 particles. The fact that an exponentially growing cycle emerges naturally from such a simple scheme demonstrates that the emergence of exponentially growing metabolisms could be simpler than previously imagined.

catalytic cycles | DNA-coated colloids | metabolism | templating

The origin of life is usually associated with self-replication, the ability of an entity to create copies of itself (1). Thus inspired, there have been many efforts in recent years aimed at creating artificial systems with self-replicative capacity. These are typically inspired by the linear chain mechanism of DNA. However, living systems are more than individual entities that can replicate themselves. Dyson (2) and Oparin (3) argued that a more critical aspect of living systems is the creation of a metabolism, a complex cascade of chemical reactions that together are able to accomplish more than any single chemical reaction can do on its own. Using a simple mathematical model, the so-called “garbage bag model,” Dyson presented a scenario through which such a complex metabolism could arise spontaneously. His idea is that a random set of catalysts will catalyze arbitrary chemical reactions in a nonsynergistic fashion. However, if each catalyst is more likely to function when there are others that are synergistic with it, then there is a critical amount of cooperativity above which metabolic cycles spontaneously emerge. This idea has been explored through abstract simulations (4). In a similar spirit, Kauffman and coworkers have shown that if the probability of one species catalyzing the formation of another is above a threshold, then catalytic cycles naturally emerge (5–7).

Whether this scenario can naturally occur in practice remains obscure. The fundamental question is to determine how likely it is for a soup of interacting catalysts to self-organize into an exponentially growing catalytic cycle. How special do the interactions between the different components need to be for spontaneous exponentially growing catalytic cycles to emerge? In this work, we present an explicit demonstration of a set of interactions in which exponentially growing catalytic cycles naturally emerge. This set of interactions models a realizable physical sys-

tem, colloidal spheres interacting with time-dependent specific interactions, in which particle clusters can template each other. The emergence of exponentially growing catalytic cycles depends on particle valences in the templating process.

We consider colloidal particles having stickers distributed uniformly over their surface. These stickers cause short-ranged, specific interactions between particles, with a programmable binding strength between pairs of particles. We have recently shown that this system has the potential of allowing high-yield equilibrium self-assembly of large structures, up to 1,000 particles (8). Classical experiments showed that DNA-based specific interactions allow assembly of crystals of nanoparticles (9–12). More recently, efforts for self-assembly at the colloidal scale have begun to bear fruit (12–18). To achieve the exponentially growing catalytic cycles of the current study, we find that it is necessary to use time-dependent interactions between the particles, whose strength can be modulated over a programmable timescale. Schemes for time-dependent interactions based on DNA hybridization exist (19), and there is already an experimental realization of a form of time-dependent interactions (20), with more under development. We will see in what follows that the timescale of the interactions plays an essential role in determining the nature of the catalytic cycles that are produced in the reactions.

Results

We define a “cluster” as a rigid structure in which any continuous deformation costs energy and in which N particles interact

Significance

Biological systems inspire a new paradigm for material synthesis, aiming to design materials that emulate living systems, providing both functionality and self-replication. Colloidal particles endowed with specific interactions provide a particularly promising approach for realizing this vision. Here, we consider a set of colloidal spheres with specific, time-dependent interactions and demonstrate that the interactions can be designed so that clusters of particles create other clusters through templating reactions. Surprisingly, simple templating rules generically give rise to the production of a sea of clusters of various sizes. The sea of clusters grows exponentially in a catalytic cycle. This is a specific realization of Dyson's notion of an exponentially growing metabolism, emerging naturally from a simple scheme.

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¹To whom correspondence should be addressed. Email: zorana.zeravcic@espci.fr.

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in our landscape (8, 21, 22, 24) and found multiple parent clusters that can efficiently catalyze the octahedron: The discussed parent catalyst is the only one with $N_0 = 7$, and multiple parents with $N_0 > 7$ can carry out the reaction efficiently (*SI Text* and Fig. S1). There is nothing special about the reaction in which the octahedron is the target; however, the choice of having particle valence larger than one strongly impacts the totality of catalytic reactions for a given parent catalyst, as we will discuss below.

The reactions of template-driven catalysis require time-dependent bond strengths: The bond strengths of the monomers binding to the catalytic cluster must weaken in time, whereas the bonds between bound monomers must strengthen in time. The dissociation timescale of the network of bound monomers is set by the timescale of the weakening bonds. By varying this timescale, it is possible to change the size of the dissociated network of monomers and hence the size of the catalyzed cluster. This process is in spirit similar to the time-dependent type of enzyme catalysis, which has been established as a common type of catalysis in biology (28). In our simulations, we implement this varying timescale by triggering the dissociation event based on the number of bonds within the monomer network. We choose the necessary number of bonds for triggering dissociation from a distribution, where moving the distribution peak toward, e.g., larger numbers corresponds to a longer dissociation timescale (*SI Text* and Fig. S2).

When the interactions are realized by DNA stickers, the monomer–catalyst binding involves complementary strands, so that for each particle species in the parent, there is a complementary particle species that can bind to it. The complementary species interact among themselves in the same way as the original species do. The catalytic system of the $N_0 = 7$ parent catalyst (Fig. 1 *CI*) is therefore defined to have double the number of species, i.e., 14 species (Fig. 24). We now proceed to test in detail the performance of the $N_0 = 7$ parent catalyst, using dissipative particle dynamics (DPD) techniques introduced previously for colloidal particles with stickers (8, 29). Our simulation contains colloidal spheres of diameter d , with an interaction range of $1.05d$. The particles are immersed into a DPD solvent of smaller particles. We simulated systems with 512 colloidal particles, out of which 7 comprise the parent catalyst. Simulations are run at a

fixed temperature with a volume fraction of colloids $\phi_{coll} = 0.01$. Fig. 2*B* shows a particular event of the parent cluster producing an octahedra in a simulation.

Emergent Catalytic Reactions. Although Fig. 2*B* demonstrates that the $N_0 = 7$ parent catalyst indeed effectively templates octahedra, a close examination of the simulations demonstrates that the cluster is also capable of templating other clusters. In turn, the clusters that are templated from the parent $N_0 = 7$ catalyst can themselves template even more clusters. The rich templating capability becomes apparent as we increase the number of monomer bonds necessary for dissociation event and thereby favor larger catalysis products. Fig. 2*C* shows a snapshot from a simulation, highlighting a few examples of clusters and nonrigid structures.

The root cause of the degenerate structures that are produced is the valence-2 particle in the $N_0 = 7$ parent catalyst. Without this valence-2 particle, only some clusters with < 7 particles can be templated (*SI Text* and Fig. S3). However, the degeneracy causes an enormous zoo of clusters to be produced by the templating reactions. To enumerate the set of possible rigid clusters that can be produced starting from the $N_0 = 7$ cluster, we take our database of cluster geometries up to 14 particles (21–23) and ask which of these geometries can be realized by using the interaction matrix of the parent $N_0 = 7$ catalyst (Fig. 1 *CI*), where multiple copies of the valence-2 particle are allowed (particle species 7). There are 100 different geometries that are consistent with this interaction matrix, from $N = 2$ to $N = 11$ particles. These give rise to a total of 176 different clusters, because some of the geometries have multiple colorings (i.e., some geometries can be constructed using different combinations of particle species). Of the 176 clusters, 135 have > 5 particles, and we focus on these.

We next ask which of the 135 clusters are capable of templating each other. Note that from here on, for simplicity of presentation, we consider clusters with complementary colorings to be one and the same; i.e., a pair of complementary particle species is regarded as a single species. This simplification does not affect any of our results and conclusions (*SI Text*). Fig. 3 shows a directed graph, where each of the 135 nodes corresponds to a rigid cluster. A (directed) edge between two nodes indicates

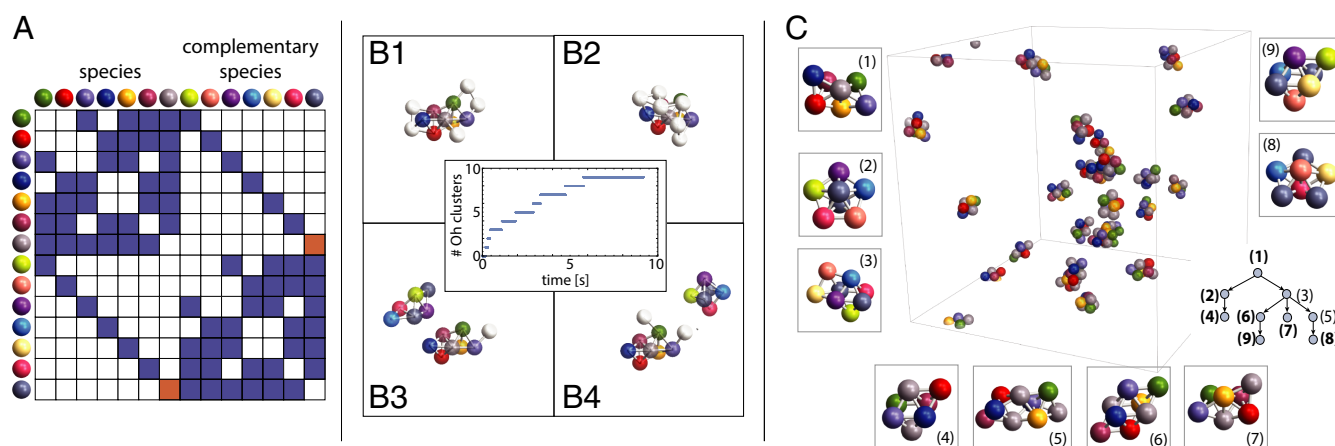


Fig. 2. (A) The interaction matrix shows that the mutual interactions among the catalyst cluster particles (the first seven rows/columns) are identical to the ones among their complementary species (the last seven rows/columns). Each particle species can bind its complementary species (off-diagonal seven by seven blocks). Orange entries mark the only interactions with valence 2. (B) Simulation of catalysis of octahedra from the $N_0 = 7$ parent catalyst. Particles in the catalyst are colored according to their interaction matrix, with the particles bound from the bath colored white (unbound particles and solvent particles are omitted for clarity). (B1–B4) Snapshots of an octahedron being formed. (B, Inset) Plot of the number of octahedra as function of time obtained in a simulation. (C) Snapshot of simulation started with a single $N_0 = 7$ catalyst (labeled 1), where all generated clusters were allowed to template other clusters. A few selected clusters (labeled 2–9) are marked, with the sequence of them getting templated shown on the right. Only clusters 3 and 5 are nonrigid structures. Clusters 3 and 6 have eight particles, cluster 5 has nine particles, and the rest have seven particles.

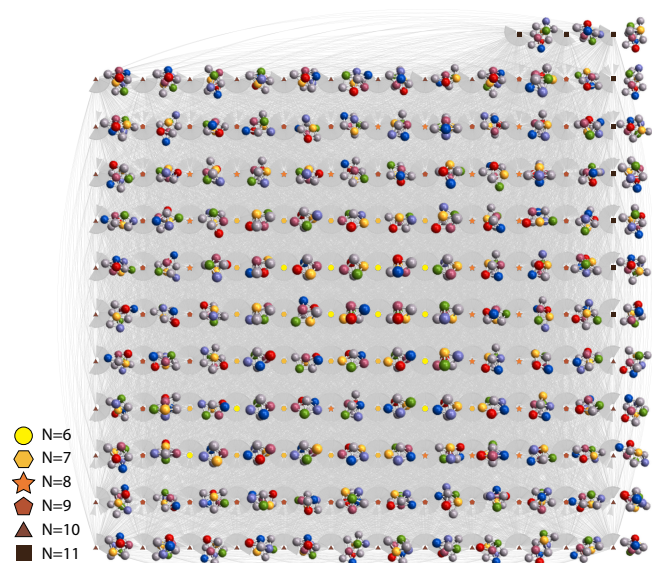


Fig. 3. Directed graph showing the templating connections between all clusters with >5 particles, realized by using the interaction matrix of the $N_0 = 7$ parent catalyst. There are 135 clusters in total.

that the initial cluster can template the target one. There are 8,057 pairs of connected clusters in the graph, so the probability of a connection between any two clusters is $\sim 90\%$. This percentage is higher than the critical value predicted by Kauffman above which catalytic cycles emerge from a reactive graph (5, 6). Indeed, there are many cycles within our graph, an example of which is shown in Fig. 4A.

To make the structure of the cycles visible, Fig. 4B reorganizes the graph in Fig. 3, grouping clusters by their size and coloring. For example, to generate a cycle with a $N = 11$ cluster starting from the parent $N_0 = 7$ catalyst, we need to template a type of $N = 8$ cluster (8 possibilities out of 24 clusters), which then templates a type of $N = 9$ cluster (31 possibilities out of 37 clusters). There are $>1.7 \times 10^6$, 1.0×10^7 , 6.2×10^8 cycles of length 3, 4, 5, respectively. The parent $N_0 = 7$ catalyst is involved in $\approx 15\%$ of the average number of cycles per cluster. The largest cycle we found has size 83 and involves the parent catalyst.

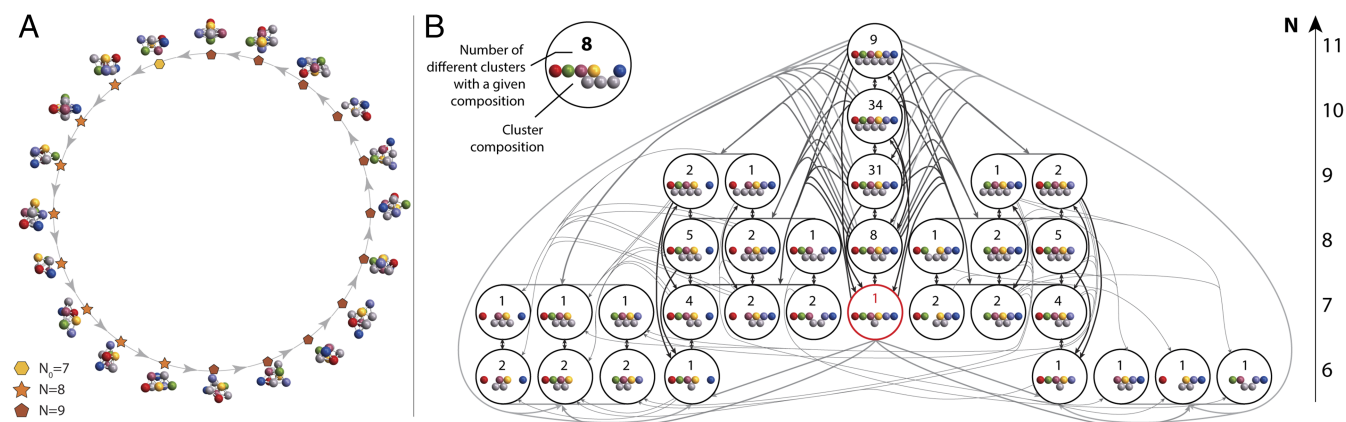


Fig. 4. (A) An example of emergent catalytic cycle that includes the $N_0 = 7$ parent catalyst. (B) The reorganization of the directed graph in Fig. 3, where clusters are grouped by their number of particles (N) and by the species of each of their particles. A directed edge from a group of clusters (a circle) to another group means that all clusters in the former can template all clusters in the latter group. When the edge has an endpoint on a horizontal line that connects several circles, it represents multiple edges to each of those circles. The group to which the $N_0 = 7$ cluster belongs is marked by a red circle.

Exponential Growth of Catalytic Cycles. Given this web of templating possibilities between the different clusters (Figs. 3 and 4B), what is the outcome when a $N_0 = 7$ catalyst is placed in a monomer bath? To answer this, let $\mathbf{c}(t)$ be a vector of probabilities, where $c_i(t)$ is the normalized concentration of the i^{th} cluster. Then,

$$\frac{d\mathbf{c}}{dt} = \mathbf{M}\mathbf{c}, \quad [1]$$

where \mathbf{M} is the matrix of first-order production rates between the different clusters, with M_{ij} representing the rate at which the j^{th} cluster templates the i^{th} cluster.

Now, M_{ij} can only be nonzero if the corresponding edge in the directed graph (Figs. 3 and 4B) is nonzero. The magnitude of M_{ij} is set by kinetic considerations: A templating reaction requires that all of the templated particles diffuse to the surface of the catalyst and then dissociate together once enough bonds between the particles are formed. The critical parameter is the timescale of dissociation, τ_{dis} , the length of time the templating particles are allowed to stay bound to the catalyst before they dissociate. The number of particles that template before dissociation increases with increasing τ_{dis} , leading to a preference for larger clusters. In contrast, if τ_{dis} is short, templating larger clusters is impossible, and the catalysts only produce small clusters.

A reasonable model chooses τ_{dis} so that templated clusters of a given size are favored, and then both larger and smaller clusters are disfavored. We model this by choosing the value of each matrix element of \mathbf{M} , i.e., the value of kinetic rate for each templating reaction, which is inversely proportional to the corresponding τ_{dis} . Given a matrix \mathbf{M} , what is the dynamics of Eq. 1, assuming that we start from a single instance of the $N_0 = 7$ catalyst? If \mathbf{c} has K components, then Eq. 1 has K eigenmodes, namely, solutions C_i^α that grow/shrink exponentially when $\text{Re}[\lambda^\alpha]$ is positive/negative, where λ^α is the corresponding eigenvalue. When we choose the kinetic rates to vary weakly (SI Text), the spectrum corresponding to our model is shown in Fig. 5A. We sort the eigenvalues so that $\text{Re}[\lambda^1]$ is the smallest and $\text{Re}[\lambda^K]$ is the largest. The same figure shows the spectrum for a different choice of kinetic rates, drawn from an exponential distribution, where kinetic rates for production of the largest clusters happen to be relatively increased (SI Text). In both cases, the λ^K is real and $\lambda^K \gg \text{Re}[\lambda^\alpha]$ for $\alpha < K$, and we find this to be a robust feature under variation of kinetic rates. This is consistent with the Perron–Frobenius theorem, which guarantees

of catalytic cycles. Instead of a single proliferating entity, our system results in exponentially growing catalytic cycles, which is reminiscent of a metabolism. Were the reactions to occur in a cell volume that itself divided in response to, e.g. the amount of one of the clusters in our cycle, we would have a natural mechanism for an exponentially growing catalytic cell cycle.

Whereas previous models realizing Dyson's metabolism are abstract (4–6), without specific physical realization, the present construction demonstrates that it is surprisingly easy for a templated set of reactions to give rise to an exponentially growing catalytic cycle. Our only caveat is that the specific nature and properties of the catalytic cycle are emergent properties of the programmed interactions and cannot easily be directly designed. The only special aspect of the system studied here is that we have a complete characterization of the energy landscape of the colloidal particles, and therefore are able to easily make the design choices for a templated catalytic reaction to emerge. However, we see no reason why similar phenomena could not emerge from other soft-matter systems, in particular, polymers or gels (31). As but one example, it is interesting to contemplate whether a system of RNA strands might be designed to lead to an exponential catalytic cycle.

We note that the basic ingredients required to experimentally realize our system are becoming available. Controlled valence of isotropic mesoscale particles has been demonstrated (18, 32). The interaction among monomers needs to strengthen in time, so that they do not aggregate in solution, but do bind to each other during time they are attached to the template. We believe that the dissociation from the template could be induced by the very process of bonding among attached monomers (33) and/or by weakening in time of the monomer–template bonds (19), both of which require consumption of energy. The weakening and breaking of monomer–template bonds might be controlled by an externally imposed (i.e., day–night) cycle for these bonds (31, 34, 35), which could set the disassociation timescale. A first step toward time-dependent interactions has been realized between nanoparticles by using complex strand-displacement reactions that rely on a DNA fuel source (20, 36).

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